SUPPLEMENTAL NEWBORN SCREENING

House Bill Number 986 (see Appendix A) was passed by the Mississippi legislature and signed by the Governor during the 2001 legislative session. This bill amends Section 41-21-203 of the Mississippi Code. In compliance with House Bill 986, the Mississippi State Department of Health offers information developed through the Genetics Advisory Committee (see Appendix B) about supplemental newborn screening tests that are available but not provided through the Department of Health. This information is mailed to clinics, hospitals, and health care providers providing prenatal care to pregnant women and to those physicians and health care providers attending newborn children. The information should be discussed and shared with all pregnant women and their families. A Supplemental Newborn Screening pamphlet is also included. This pamphlet should be given to the expectant mother during her pregnancy and must be given to her again when she gives birth, as required by House Bill 986. Additional pamphlets are available upon request through the Division of Genetic Services.

Supplemental Newborn Testing covers over 30 inherited disorders (see Appendix C). Although these disorders are rare, they are serious and some of them are life-threatening. Because most of these disorders are inborn chemical problems, they cannot be "cured." However, the serious effects of many of these disorders can be lessened if a special diet, medical treatment, or other method of intervention is started soon after birth.

Most supplemental genetic test results are acquired through the use of a tandem mass spectrometer (often abbreviated as MS/MS). A tandem mass spectrometer is one of several types of analytical instruments known as mass spectrometers. Mass spectrometers are used to analyze thousands of compounds such as those present in our bodies, our medications, the environment, manufactured materials, foods, and poisons. A tandem mass spectrometer is two mass spectrometers in series connected by a chamber known as a collision cell. The specimen sample to be analyzed is sorted and "electronically" weighed in the first mass spectrometer, then broken into pieces in the collision cell, and the pieces are then sorted and weighed again in the second mass spectrometer. Since every molecule has a unique mass (i.e., weight), the tandem mass spectrometer can identify a compound by its mass and determine how much of the compound is present.

The compounds in the blood of infants tested using tandem mass spectrometry are known as amino acids and acylcarnitines. Amino acids are the building blocks of proteins that become the important parts of our tissues, muscles, organs, blood. Carnitine is a transportation system for fats in and out of the cell's energy factory, the mitochondria. When a fat (as a fatty acid) is attached to carnitine it is called an acylcarnitine. Acylcarnitines are often identified by the size of the fat molecule attached. These may be categorized simply as short, medium and long chain fats or denoted by a combination of letters and numbers. For example, the important medium-sized fat attached to carnitine that is measured in the disorder MCAD (medium chain acylCoA dehydrogenase) deficiency is an eight-carbon fatty acid known as octanoylcarnitine and abbreviated as C8. The tandem mass spectrometer can weigh this molecule and all of the other acylcarnitines as well to tell us how much is present. The results produced by the mass spectrometer display the data as vertical lines distributed across a horizontal axis (called a mass

spectrum). Where the vertical line occurs in the spectrum identifies a compound's mass while the height of the line represents how much of the compound is present. The capability of tandem mass spectrometry to identify genetic disorders such as MCAD (which has an incidence of 1:16,000 and if undetected can result in the sudden death of a previously healthy appearing child who fasts for longer than 12 hours) makes Supplemental Newborn Screening an important consideration for parents.

Tandem mass spectrometers are complex instruments. The methods used to prepare the samples for analysis by mass spectrometry require specialized reagents. Although tandem mass spectrometry is often called a simple blood test, it is not a simple method. Tandem mass spectrometry requires several expert scientists to perform analyses and medical experts to interpret the large amount of clinical data produced from the analysis of a blood sample. The instruments are expensive and to achieve appropriate cost/benefit for analyses of blood samples, a laboratory must screen many tens of thousands of samples per year. But in qualified laboratories that have sufficient experience with the technology, tandem mass spectrometry can expand newborn screening by testing for many disorders that are not included in most standard newborn test batteries.

In Mississippi, state law requires that newborns be tested for phenylketonuria, galactosemia, hypothyroidism, and hemoglobinopathies. On January 1, 2002, testing for congenital adrenal hyperplasia will also be required (see Appendix D and the enclosed pamphlet). The Mississippi State Department of Health provides all these required tests.

Only newborn screening tests required by law are provided through the State Department of Health. Supplemental Newborn Screening can be obtained through other qualified laboratories for a nominal fee. **Parents must be informed that they can request Supplemental Newborn Screening from their child's physician. They should be provided with, or have access to, sufficient information to allow them to make an informed decision. If they choose to have this test done, they should arrange in advance with their physician for the blood sample to be collected at the same time as the state-required newborn screening blood sample is collected.** The optimal time to collect both specimens is while the baby is in the hospital and at least 24 hours after delivery.

Payment for the Supplemental Newborn Screening test should usually accompany the specimen. Referrals for additional follow-up should be made for all inconclusive or abnormal test results. The fee for the initial supplemental screening is not currently covered by private insurance companies or Mississippi health benefits (which includes the Children's Health Insurance Program (CHIP) and Medicaid).

Supplemental Newborn Screening pamphlets can be obtained by contacting:

Mississippi State Department of Health
Division of Genetic Services
P.O. Box 1700
Jackson, MS 39215-1700
Phone 601-576-7619, Fax 601-576-7498

Additional information can be requested from the laboratories that offer Supplemental Newborn Screening with tandem mass spectrometry. Two of the more publicized laboratories are:

Baylor University Medical Center
Institute of Metabolic Disease
Mass Spectrometry and Biochemical Diagnostic Unit
3812 Elm Street
Dallas, TX 75226
Phone 214-820-4500 or 1-800-422-9567 (1-800-4- BAYLOR), Fax 214- 820-4853
Internet: www.baylorhealth.com/newbornscreening

Neo Gen Screening
P.O. Box 219
90 Emerson Lane
Bridgeville, PA 15017
Phone 866- 463-6436 or 1-866-463-6436 (1-800-4-NEOGEN)
Internet: www.neogenscreening.com

Or contact:

Hans-Georg O. Bock, M.D., Ph.D., F.A.C.M.G.
University of Mississippi Medical Center
Division of Medical Genetics
Department of Preventive Medicine
2500 North State Street
Jackson, MS 39216
Phone 601-984-1900, Fax 601-984-1916

House Bill No. 986
(As Sent to Governor)

AN ACT T0 AMEND SECTION 41-21-203, MISSISSIPPI CODE OF 1972, TO REQUIRE HEALTH CARE PROVIDERS PROVIDING PRENATAL CARE TO A PREGNANT WOMAN TO NOTIFY THE WOMAN THAT THERE ARE NEWBORN SCREENING TESTS AVAILABLE THAT MAY BE GIVEN TO HER CHILD IN ADDITION TO THE TESTS REQUIRED BY THE STATE, AND TO PROVIDE TO THE WOMAN THE MOST RECENT INFORMATION OF THE HEALTH DEPARTMENT REGARDING THOSE TESTS; TO REQUIRE THE PHYSICIAN OR OTHER HEALTH CARE PROVIDER ATTENDING A NEWBORN CHILD TO NOTIFY THE PARENTS THAT THERE ARE NEWBORN SCREENING TESTS AVAILABLE THAT MAY BE GIVEN TO THE CHILD IN ADDITION TO THE TESTS REQUIRED BY THE STATE, AND TO PROVIDE THE PARENTS THE MOST RECENT INFORMATION OF THE HEALTH DEPARTMENT REGARDING THOSE TESTS; TO AMEND SECTION 41-21-201, MISSISSIPPI CODE OF 1972, AS AMENDED BY SENATE BILL NO. 2210, 2001 REGULAR SESSION, TO REQUIRE THE STATE DEPARTMENT OF HEALTH TO DEVELOP INFORMATION MATERIALS ABOUT NEWBORN SCREENING TESTS THAT ARE AVAILABLE, WHICH SHALL BE USED BY PHYSICIANS AND OTHERS TO PROVIDE THE REQUIRED INFORMATION TO PREGNANT WOMEN AND PARENTS UNDER SECTION 41-21-203; TO AUTHORIZE THE STATE DEPARTMENT OF HEALTH TO PROVIDE FOR TESTING FOR CONGENITAL ADRENAL HYPERPLASIA (CAH) AS PART OF ITS NEWBORN SCREENING PROGRAM; AND FOR RELATED PURPOSES.

BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF MISSISSIPPI:

SECTION 1. Section 41-21-203, Mississippi Code of 1972, is amended as follows:

41-21-203. (1) * * * The physician attending a newborn child or the person attending a newborn child * * * shall provide the child tests that have been approved by the State Board of Health. However, no such tests shall be given to any child whose parents object thereto on the grounds that the test conflicts with his religious practices or tenets. The State Department of Health shall follow up all positive tests with the attending physician who notified the department thereof, or with the parents of the newborn child when the notification was made by a person other than a physician. When a test is confirmed, the services and facilities of the State Department of Health and those of other

state boards, departments and agencies cooperating with the State Department of Health in carrying out the program shall be made available to the extent needed by the physician.

(2) In addition to the requirements of subsection (1) of this section, (a) any clinic, hospital, physician or health care provider providing prenatal care to a pregnant woman shall notify the woman that there are newborn screening tests available that may be given to her child in addition to the tests that are required by the state, and shall provide to the woman the most recent information developed by the State Department of Health regarding these tests; and (b) the physician or other health care provider attending a newborn child shall notify the parents that there are newborn screening tests available that may be given to the child in addition to the tests that are required by the state, and shall provide to the parents the most recent information developed by the State Department of Health regarding these tests.

SECTION 2. Section 41-21-201, Mississippi Code of 1972, as amended by Senate Bill No. 2210, 2001 Regular Session, is amended as follows:

41-21-201. (1) The State Department of Health is * * * authorized to establish, maintain and carry out a newborn screening program designed to detect hypothyroidism, phenylketonuria (PKU), hemoglobinopathy, congenital adrenal hyperplasia (CAH) and galactosemia which may result in mental retardation or medical complications in children. The State Board of Health is authorized to adopt rules and regulations necessary to accomplish the program.

(2) Not later than October 1, 2001, the State Department of Health shall develop information materials about newborn screening tests that are available, which shall be used by physicians and others to provide the required information to pregnant women and parents under Section 41-21-203.

SECTION 3. This act shall take effect and be in force from and after July 1, 2001.

Genetics Advisory Committee
August 14, 2001

Hans-Georg O. Bock, M.D.
University of Mississippi Medical Center
Division of Medical Genetics
Department of Preventive Medicine

William Roberts, M.D.
University of Mississippi Medical Center
School of Medicine

William Sorey, M.D.
University of Mississippi Medical Center
Department of Pediatrics

Chris Friedrick, M.D.
University of Mississippi Medical Center
Division of Medical Genetics
Department of Preventive Medicine

Kimbel Shephard, M.D.
Northeast Mississippi Pediatrics

Mary Patterson
Mississippi Hospital Association

Geneva Cannon, B.S.R.N., M.H.S.
Office of Insurance

William Sistrunk, M.D.
Mississippi Academy of Pediatrics

Margie Cox, M.S.W.
The University of Southern Mississippi
Institute for Disability Studies

Mitchell Hudspeath
Parent

SUPPLEMENTAL NEWBORN SCREENING LIST OF DISORDERS*

	Abbreviation
ARGININEMIA	
ARGININOSUCCINATE LYASE DEFICIENCY	ASA
CARNITINE PALMITOYLTRANSFERASE II DEFICIENCY	CPT II
CARNITINE/ACYLCARNITINE TRANSLOCASE DEFICIENCY	TRANSLOCASE
CITRULLINEMIA	
GLUTARIC ACIDURIA TYPE I	GA I
HOMOCYSTINURIA: CYSTATHIONINE SYNTHASE DEFICIENCY	
3-HYDROXY-3-METHYLGLUTARYL-CoA LYASE DEFICIENCY	HMG
HYPERAMMONEMIA, HYPERORNITHINEMIA, HOMOCITRULLINURIA SYNDROME	HHH
HYPERMETHIONINEMIA	
ISOBUTYRYL-CoA DEHYDROGENASE DEFICIENCY	
ISOVALERIC ACIDEMIA	IVA
LONG-CHAIN HYDROXYACYL-CoA DEHYDROGENASE DEFICIENCY	LCHAD
MALONIC ACIDURIA	
MAPLE SYRUP URINE DISEASE	MSUD
MEDIUM-CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY	MCAD
2-METHYLBUTYRYL-CoA DEHYDROGENASE DEFICIENCY	
3-METHYLCROTONYL-CoA CARBOXYLASE DEFICIENCY	MCC DEF
METHYLMALONIC ACIDEMIA	MMA
MITOCHONDRIAL ACETOACETYL-CoA THIOLASE DEFICIENCY	THIOLASE
MULTIPLE ACYL-CoA DEHYDROGENASE DEFICIENCY	MADD, GA II
NONKETOTIC HYPERGLYCINEMIA	NKH
5-OXOPROLINURIA	
PHENYLKETONURIA	PKU
PROPIONIC ACIDEMIA	PPA
SHORT-CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY	SCAD
TRIFUNCTIONAL PROTEIN DEFICIENCY	
TYROSINEMIA TYPE I	TYR I
TYROSINEMIA TYPE II	TYR II
VERY LONG-CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY	VLCAD

*Specific disorders screened depends on the laboratory of choice

As required by the birth defects registry Law, Section 41-21-205 of the Mississippi Code, all <u>confirmed</u> cases of genetic disorders must be reported to the Mississippi State Department of Health.

08/01/01

Mississippi State Department of Health
Congenital Adrenal Hyperplasia (CAH)

In 1988 the Mississippi State Department of Health was authorized to conduct certain newborn screening tests by Senate Bill No. 2299, an act to amend sections 41-21-201 and 41-21-203 of the Mississippi Code of 1972. As a result of this legislation, newborns born in the State of Mississippi are currently screened for galactosemia, congenital hypothyroidism, phenylketonuria (PKU), and hemoglobinopathies such as sickle cell anemia, thalasemia, and sickle-C disease.

Beginning January 1, 2002, newborns will also be tested for congenital adrenal hyperplasia (CAH). This additional test is mandated by House Bill 986. CAH is a genetic endocrine disorder caused primarily by a deficiency of enzymes needed for the adrenal glands to make the hormones cortisol and aldosterone. This enzyme defect is identified by testing for the level of 17-alpha-hydroxy-progesterone (17-OHP) in dried blood spots.

Cortisol is a steroid hormone. Cortisol is needed by the body to:

- maintain blood sugar levels
- maintain body fluids and electrolytes
- protect the body against stress

The absence of cortisol leads to pituitary hyperfunction and an increase in the size (hyperplasia) of the adrenal glands.

Aldosterone is a hormone that controls the salt levels in the blood. When the amount of aldosterone is too low, salt levels in the blood fall, as does total body water.

CAH can also cause excess production of adrenal androgens. These are hormones that are secreted in both males and females during fetal life, decreasing at three to six months after birth and resuming during puberty. Increased androgen levels can result in masculinization of female genitalia.

Infants with CAH can die shortly after birth as a result of circulatory collapse and salt-losing crisis. Early diagnosis and treatment of CAH can prevent adrenal crisis and early infant death. CAH cannot be cured but can be effectively treated by administering cortisol and salt-retaining hormone medications, initiated and monitored by pediatric endocrinologists.

According to literature, CAH is seen in 1 in 15,000 births and has been added to the newborn screening panel in about 20 states nationwide. The MSDH newborn screening program currently contracts with the Tennessee Department of Health to perform the four screening tests mandated by the Mississippi legislature. Tennessee began CAH screening for infants in 2000, and the Tennessee State Lab is prepared to test specimens submitted from Mississippi for CAH. Data from Tennessee and other southeastern states testing for

CAH indicate that false positives can be expected, with the ratio of false to true positive to range from 70:1 to 100:1. **The normal cutoff values for CAH are weight dependent. It is crucial to include birth weights for newborns and current weights for repeat tests when submitting specimens for CAH testing**. The lab will not know if 17-OHP is elevated unless the weight is known.

Goals for screening newborns for CAH in Mississippi will be to identify all infants with the salt-losing form and treat within the first week of life, and to correct gender assignment in affected females with ambiguous genitalia. The Tennessee lab phones all presumptive positive tests to the MSDH Division of Genetic Services. The doctor of record is notified of the abnormal test results, and local MSDH staff assist in contacting the family and arranging for follow-up. The infant should be evaluated immediately and observed until electrolytes are known to be normal. If electrolytes are abnormal, the infant will require hospital admission and IV fluids.

Questions regarding CAH testing and follow-up protocols should be addressed to:

Mississippi State Department of Health
Division of Genetic Services
P.O. Box 1700
Jackson, MS 39215-1700
Phone 601-576-7619, Fax 601-576-7498

References

American Academy of Pediatrics: Section on Endocrinology and Committee on Genetics. "Technical Report: Congenital Adrenal Hyperplasia.." *Pediatrics* Vol. 106 No. 6, December 2000, 1511-1518.

Chace, Dr. Donald H., Ph.D., M.S.F.S. "Tandem Mass Spectrometry and Newborn Screening." Neo Gen Screening. Internet: www.neogenscreening.com.

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March of Dimes. "Core Group of Newborn Screening Tests Recommended By The March Of Dimes." Internet: www.modimes.org/About2/PressReleases/CurrentPressReleases/TestRecommended.htm.